THE ROLE OF CERTAIN SUBCORTICAL FORMATIONS IN THE DEVELOPMENT OF ADAPTATION TO OXYGEN DEFICIENCY

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ABSTRACT: In white mice before and after adaptation to chronic hypoxia, disorders occurred in the various subcortical formations of the brain. It was shown that disorders in the reticular formation of the pons with encroachment by the nucleus reticularis tegmenti both before and after adaptation promotes an increase in the survival of rats at an altitude of 12,500 m. Disorders in the brain in the region of the ventromediothalamus and of the posterior hypothalamus promotes an increase in the tolerance of animals to acute hypoxia. Disorders in the region of the anterior hypothalamus before adaptation of the animals increases their altitude tolerance and after adaptation, lowers it.

Oxygen deficiency is a factor that man must encounter under /143
the most varying conditions. At the present time, a rather large amount of material has been accumulated concerning changes in the organism caused mainly by hypoxia and hypoxemia. However, in spite of the studies which have been carried out for many years on the problem of adaptation of an organism to oxygen deficiency, at the present time there is still no unified concept on the question of the mechanisms which lie as a basis of this. Study of materials which were available in the literature result on the conclusion that adaptation to hypoxia should be studied as a part of the overall problem of compensation of the functions which are accomplished under the regulating influence of the central nervous /144
system. Mainly, in this plan, we find an almost complete lack of data on the role of the different structures of the brain in the mechanisms of development and compensation both of acute and especially of chronic oxygen deficiency.

Taking into account the importance of the reticular formation, the thalamus and the hypothalamus in the mechanisms of the brain's activity and also data on the hypothalamus as an apparatus associated with the formation of specific and non-specific reactions such as "stress", we carried out an experimental study of the role of the above regions of the brain in the adaptation of an organism to oxygen deficiency.

The work was carried out on white rats. Using a stereotaxic apparatus in the experimental rats, we electrolytically interrupted the reticular formation of the brain or the anterior hypo-

thalamus or the posterior hypothalamus and also the thalamus of the ventromedial dorsal, ventral and medial hypothalamus. In the control animals, we carried out the operation without disruption.

As a function of the series the operation was carried out prior to adaptation of the animals to chronic hypoxia or after it.

The animals were adapted in the pressure chamber by daily ascents from 4000 to 5000 m with a 7-hour exposure. The duration of adaptation consisted of 15-30 days. Part of the animals were adapted around the clock for a period of 15 days. Then the animals were tested for survival and conditions of acute hypoxia created in the pressure chamber by ascent to an "altitude" of 12,500 m. The chamber had a glass front wall which permitted us to carefully follow the behavior of the animals. The criterion of survival in all experiments was the last breath.

The control animals were intact rats who were subjected to adaptation along with the experimental animals. The choice of data from the experiments for statistical treatment was carried out on the basis of a histological control of localization of the disorder.

In the series of experiments in explaining the role of the reticular formation we obtained statistically reliable data which indicate that disruptions in the region of the reticular formation of the brain and the nuclei and the nucleus reticularis tegmenti carried out both before adaptation and after facilitates an increase in the survival of the rats at an "altitude" of 12,500 m. In those cases when the disorder was insignificant and occurred only with a change in the morphological structure of the nerve cells, the lifetime at an "altitude" of 12,500 m was approximately the same as in the control adapted rats.

It is known that with injury to the reticular formation the reaction of awakening is sharply weakened or is completely lacking. In this case probably the tonus of the cortex caused by the normally functioning reticular formation is weakened and consequently a stable functional state of the cortex is created with respect to the action of the stimuli emitted by the numerous receptors, i.e., the sensitivity of the cerebral cortex is lowered. From this point of view our data agree with the literature data in that /145 the slowing down of the cortex or its absence facilitates an increase in tolerance to oxygen deficiency. On the other hand, G. Megun concludes that the stress-stimuli stimulate the hypothalamus-hypophesis-adrenal system through the reticular formation and therefore it is quite probable by introducing a disruption into the reticular formation we can remove the stress from the system by averting its exhaustion and in the same way we can facilitate a better adaptation to chronic oxygen deficiency. In this respect the data of Hazen and Gügenar are of interest since

they indicate that the limit of tolerance to hypoxia is determined by the condition of the nervous and humoral regulator system and by all of the characteristics in the course of the exchange processes. Hence the tactics of the prophylactic intervention must be determined by arrangements which permit knowing beforehand the exhaustion first of all of the nervous regulator mechanisms and also the humoral regulator mechanisms.

Our data also agree with this concept on disorder in the region of the ventro-medial thalamus and the posterior hypothalamus. Analysis of the experimental data obtained during the disorder of the posterior hypothalamus prior to adaptation to chronic hypoxia and after reveals a tendency for increase in survival of the animals at an "altitude" of 12,500 m. With disruption in the region of the ventro-medial thalamus the lifetime of the experimental rats under the conditions of acute hypoxia is almost twice that in the control animals. In the opinion of Bremer, Morutstsi and Megun, Rossi and Tsanketi, both the posterior hypothalamus and the ventro-medial thalamus are a part of the ascending activating system and emit to the cortex tonic discharges just as the reticular formation.

Disruptions which were applied to the anterior hypothalamus with encroachment by the area hypothalamica anterior, the nucleus paraventricularis and the lateral nuclei facilitated better adaptation to hypoxia. This is also indicated by the statistically valid data on survival by experimental rats of the control group at an "altitude" of 12,500 m ($t = 3.5$). The average time of survival of the experimental rats is 17.1 minutes, that of the control animals 7.1 minutes, i.e., 2.5 times as large. According to the data of Gess, Zager, et al., it is mainly this region of the hypothalamus which has a relationship to the specific forms of exchange and also to regulation of the numerous functions of the endocrine glands which participate in the specific forms of the exchange. In this respect we may assume that disorder in the anterior hypothalamus is accompanied by substantial changes in the exchange process which in final account change the overall reaction of the organism, in particular its tolerance to acute oxygen starvation. And if we take into account that, as a result of disorder in the anterior hypothalamus, this is reduced to a change in the liberation of the ACTH for change in the secretion of the /146
adrenal glands of the corticoids and adrenalin, then apparently we can also include the sympato-adrenal system which recently has received considerable attention.

It is interesting that in the series of experiments in which the anterior hypothalamus underwent disorders after onset of adaptation the animals died under conditions of acute hypoxia earlier than the control animals; disorder in this case was localized in the anterior hypothalamus with encroachment by the supraoptic or the paraventricular nuclei and in certain instances by the preoptic medial region. The average time of survival of the

experimental rats was 4.34 minutes, and that of the control animals 7.8 minutes ($P > 0.05$). According to the data of Barbashovaya, the demodulation of the adrenal glands is not an obstacle for acclimatization to hypoxia but an adrenalectomy substantially decreases the adaptation to acute hypoxia and acclimatization does not occur. It was established that stimulation at average elevation excites secretion of the oxycorticoids.

Disorder in the anterior hypothalamus lowers the secretion of the ACTH to the effect of trauma. Since we assume that in the formation of compensation to hypoxia there is a participation of the system of hypothalamus-hypophesis-adrenal, then an intervention in the form of a disorder in the blocking separation of the ACTH, and in the same way, a disturbing intactness of the reflector apparatus, is compiled in the organism in the process of adaptation, lowers the tolerance of the organism and leads to a more rapid death in comparison with the control animals.

Disorder in the posterior part of the thalamus in the rats who were adapted to oxygen deficiency lowers the tolerance to hypoxia. The difference in lifetime between experimental animals and the control animals is statistically proven ($P > 0.01$).

Thus in the regulation of the function in the process of adaptation to hypoxia along with the cerebral cortex substantial significance is attributed to the subcutaneous formation which is indicated by the factual material obtained that permits making the following conclusion:

1. With disorder in the reticular formation in the region of the brain and the nucleus reticularis tegmenti of the anterior hypothalamus the adaptation to chronic hypoxia occurs more effectively.

2. Disorder in the reticular formation of the brain and the nucleus reticularis tegmenti of the posterior hypothalamus, the ventro-medial thalamus in animals adapted to hypoxia substantially increases their tolerance to acute hypoxia.

3. Disorder in the anterior hypothalamus and the dorsal thalamus after adaptation to hypoxia lowers the altitude tolerance of the animal.